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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,130	11/18/2003	Matthias Straub	029300.51815US	1917

23911 7590 07/18/2005

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EXAMINER	
HENLEY III, RAYMOND J	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,130	STRAUB ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-7 and 10-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-7 and 10-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 4-7 AND 10-24 ARE PRESENTED FOR EXAMINATION

The indicated allowability of claims 4-7 and 10-24 is withdrawn in view of the newly discovered references to Chiou et al (Journal of Clinical Pharmacology), Bugrii et al. (Medline Abstract Only, Accession No. 87019503), U.S. Patent No. 6,026,817 (Clemens) and U.S. Patent No. 6,790,463 (Hofmann et al.), each newly cited by the Examiner. The delay in the citation and application of these references is regretted. Rejections based on the newly cited references follow.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention." (MPEP 2173).

The term "about" in the expressions of claims 11-15, for example "about 8 to about 12 minutes" (claim 11, line 9) is a relative term which renders the claim indefinite. The expression

"about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Because the term "about" has not been defined in a clear, objective manner, it would require subjective interpretations of whether or not a particular period of time is included by or excluded from the present claims. It is therefore the Examiner's position that the public would not be informed of the boundaries of what constitutes infringement of the present claims and thus the claims fail to meet either the tenor or express requirements of 35 U.S.C. § 112, second paragraph and are properly rejected.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-7 and 10-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schoen et al. (U.S. Patent No. 4,550,112 "Schoen '112", already of record), Schoen et al. (U.S. Patent No. 4,912,113 "Schoen '113", already of record) in view of Schoen et al. (U.S. Patent No. 5,324,732 "Schoen '732", already of record), Chiou et al (Journal of Clinical Pharmacology), Bugrii et al. (Medline Abstract Only, Accession No. 87019503), U.S. Patent No. 6,026,817 (Clemens) and U.S. Patent No. 6,790,463 (Hofmann et al.), each newly cited by the Examiner and cited on the attached form PTO-892.

Schoen '112 and '113 teach a method of treating arrhythmias which comprises the administration of 3,7-diazabicyclo(3.3.1)nonane compounds of the type claimed to a human in need thereof (see Schoen '112 at col. 5, lines 6-68 and col. 11, lines 7-25 and Schoen '113 at col. 1, line 26 - col. 2, line 26 and col. 12, line 61 – col. 13, line 14, line 28). The administration may be orally (claim 1 encompasses oral administration) or parenterally and liquid dosage forms are taught therefor (Schoen '112 at col. 14, lines 17-37 and Schoen '113 at col. 14, lines 29-48).

The differences between the above and the claimed subject matter lay in that the primary references fail to highlight:

(1) the claimed dosage regimen;

(2) the claimed fumaric salt (e.g., claim 21); and

(3) the specific types of arrhythmias (claim 5);

However, to the skilled artisan, the claimed subject matter would have been obvious because:

(1) Given that both primary references teach oral or parenteral administration in general, it would have been appreciated by the skilled artisan that two step administration of two

continuous administration phases would have been obvious and well within the teachings of the references.

Further, two-step administration of two continuous administration phases in the manner presently claimed would also have been obvious and the skilled artisan would have been motivated to administer multiple dosages depending on the response of the patient being treated. That is, if the patient does not respond to the first dosage administration, a second administration would be required. The term "continuous" in the claims can be reasonably interpreted as being that time from beginning to end of administration.

Further, while the timing of administration as in present claims 11-15 is not highlighted, such is also believed to have been obvious. "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" (see MPEP 2144.05(II)). The determination of the optimum dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art and such determination would have been made in accordance with a variety of factors. These would have included the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, the dosage regimen,

which includes the period of time for administration, that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts are not seen to be inconsistent the dosages that would have been determined by the skilled artisan.

Further, two step administration of two "continuous" administration phases for a variety of drugs was a concept well known in the art, including the cardiology art. Thus, in the treatment of patients suffering from frequent ventricular extrasystole, Bugrii et al. teach that a two step administration, i.e., a priming dose of 500 mg followed by a maintenance dose of 200 mg, of etmozine was effective (see the entire Medline abstract; an English language translation will be provided when available). Also, in Hoffman et al., it is reported in Examples 6 and 7 (cols. 9-10) that step wise administration of various dosages of medicaments was effective for the treatment of cardiac patients, e.g., "The dosage was 0.5 cc progressing to 1.0 cc in 0.1 cc steps, diluted in 100 cc sterile normal saline, infused over 20 minutes." (col. 9, lines 56-58). Further, Clemens shows that in cardiac patients, i.e., humans suffering from Coronary Heart Disease Risk Factor (CHDRF) Syndrome (see the abstract), "For a period of one to four weeks, the drug is administered at a high priming dosage. Thereafter, the drug is administered at a lower maintenance dosage." (col. 6, lines 46-49). Finally, Chiou et al. teach a means to determine optimum dosage rates and teach "One of the most common methods of drug administration is the multiple short-term intravenous infusion in which a drug is often infused at a constant rate for several minutes up to 1 or 2 hours at the beginning of each dosing interval. (page 266, col. 1, middle of the column) and that "it is concluded that the simplified method

proposed in this paper for dosage individualization in patients receiving short-term intravenous infusion should be applicable to most drugs." (page 270, col. 2, near the bottom).

Given the above, it is not seen that the presently claimed dosage regimen is critical. The data at pages 15-49 of the specification have been carefully considered, but do not diminish the propriety of the present rejection. The data appears to only indicate that method of administration is safe and effective, which would have been expected by one of ordinary skill in the art. Also, only single drug has been tested and it has not been established that such drug is reasonable representative of the entire genus of compounds present in the claims.

2) Schoen '112 at col. 6, line 14 and Schoen '113 at col. 7, line 7 specifically teach that fumaric acid salts may be employed while Schoen '732 teaches that the specifically claimed fumaric salt was known to be a pharmaceutically acceptable salt (col. 2, lines14-32).

(3) As noted above, Schoen '112 and Schoen '113 teach the treatment of arrhythmias in general and thus would have encompassed the specific arrhythmias claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-7 and 10-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/894,364 in view of Chiou et al (Journal of Clinical Pharmacology), Bugrii et al. (Medline Abstract Only, Accession No. 87019503), U.S. Patent No. 6,026,817 (Clemens) and U.S. Patent No. 6,790,463 (Hofmann et al.), each newly cited by the Examiner and cited on the attached form PTO-892. This rejection has been re-instated because it is now not the only remaining issue.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the two step administration of two continuous administration phases of the type claim would have been suggested by the art. Further, two-step administration of two continuous administration phases in the manner presently claimed would also have been obvious and the skilled artisan would have been motivated to administer multiple dosages depending on the response of the patient being treated. That is, if the patient does not respond to the first dosage administration, a second administration would be required. The term "continuous" in the claims can be reasonably interpreted as being that time from beginning to end of administration.

Further, while the timing of administration as in present claims 11-15 is not highlighted, such is also believed to have been obvious. "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" (see MPEP 2144.05(II)). The determination of the optimum

dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art and such determination would have been made in accordance with a variety of factors. These would have included the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, the dosage regimen, which includes the period of time for administration, that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts are not seen to be inconsistent the dosages that would have been determined by the skilled artisan.

Further, two step administration of two "continuous" administration phases for a variety of drugs was a concept well known in the art, including the cardiology art. Thus, in the treatment of patients suffering from frequent ventricular extrasystole, Bugrii et al. teach that a two step administration, i.e., a priming dose of 500 mg followed by a maintenance dose of 200 mg, of etmozine was effective (see the entire Medline abstract; an English language translation will be provided when available). Also, in Hoffman et al., it is reported in Examples 6 and 7 (cols. 9-10) that step wise administration of various dosages of medicaments was effective for the treatment of cardiac patients, e.g., "The dosage was 0.5 cc progressing to 1.0 cc in 0.1 cc steps, diluted in 100 cc sterile normal saline, infused over 20 minutes." (col. 9, lines 56-58). Further, Clemens shows that in cardiac patients, i.e., humans suffering from Coronary Heart Disease Risk Factor (CHDRF) Syndrome (see the abstract), "For a period of one to four weeks,

the drug is administered at a high priming dosage. Thereafter, the drug is administered at a lower maintenance dosage." (col. 6, lines 46-49). Finally, Chiou et al. teach a means to determine optimum dosage rates and teach "One of the most common methods of drug administration is the multiple short-term intravenous infusion in which a drug is often infused at a constant rate for several minutes up to 1 or 2 hours at the beginning of each dosing interval. (page 266, col. 1, middle of the column) and that "it is concluded that the simplified method proposed in this paper for dosage individualization in patients receiving short-term intravenous infusion should be applicable to most drugs." (page 270, col. 2, near the bottom).

Also, while host of the co-pending claims is limited to a male human patient, such is not seen to provide a patentable distinction because in the present claims the host may be "a human" in general and thus would include a human male.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

July 8, 2005